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THE CORNEA AND SCLERA

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CHAPTER CONTENTS

OVERVIEW OF THE EYE

The eye is the specialized organ that allows light energy from the environment to be converted to a neural signal that is passed down the optic nerve to higher brain centres. All other structures of the eye function to support this one basic function, whether this is by providing nourishment, focussing of images or protection.

The structures that form the eyeball are shown in Figure 2.1. The wall of the eyeball can be considered as being formed by three layers, or coats. The outer layer is formed by the cornea and sclera which, in general terms, provides strength to the eyeball. This outer fibrous coat provides the site for attachment of extraocular muscles as well as provides protection for the contents of the globe. It is also important for maintaining the shape of the eyeball. The middle vascular layer is comprised of the uvea (from the latin word uva meaning grape) and is principally important for providing nourishment to surrounding structures. The uveal tract consists of the iris, ciliary body and choroid. The most inner layer consists of the retina, which contains the neurons that allow light to be converted to neural signals. In addition, there are two chambers within the eyeball: the anterior chamber is located between the cornea and iris and contains aqueous humour. The posterior chamber is located behind the lens of the eye and contains the vitreous body. Below, each of these layers are considered in turn.

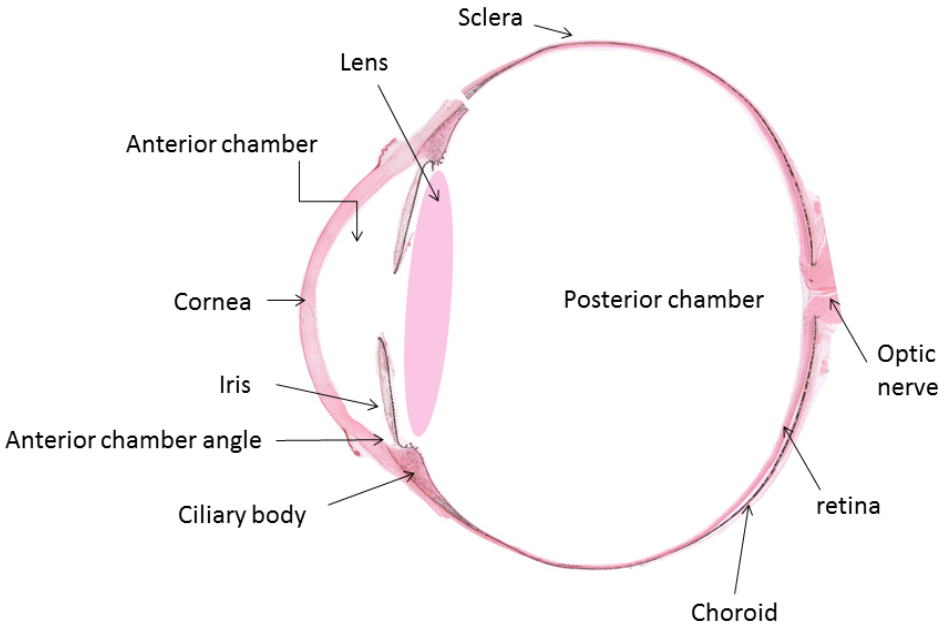


Figure 2.1. *Cross section of the monkey eye, showing the important structures that will be discussed in the sections below.*

SCLERA

The outer fibrous coat is formed by the sclera and cornea. Approximately 5/6th of the outer coat of the eyeball is covered by the sclera (comes from the greek word meaning "hard"). The sclera is largely avascular except for vessels passing through to the interior eye, and appears opaque and white in the adult. The sclera is thickest posteriorly (~1mm) and thinnest behind the insertions of tendons associated with the extraocular muscles (~0.3-0.4mm). The sclera consists primarily of dense collagen fibres (mostly collagen type I and III), although some elastic fibres are also present. The collagen fibres varying in diameter and are arranged in an irregular fashion across the sclera. Notably, the collagen fibrils are aligned with the direction of greatest tensile strength; bundles of collagen fibrils are arranged in whorl, particularly around the insertions of extraocular muscles. The arrangement of the outer collagen fibrils in this whorl like fashion is thought to be important in contributing in the tensile strength of the sclera.

When the outer coat of the eyeball is viewed in cross section, three layers of the sclera can be viewed histologically. The outer *episclera* is formed by loose connective and elastic tissue on the outer surface of the sclera. It is denser in the deeper layers and continuous with the *sclera proper.* Unlike the sclera, the episclera contains numerous small blood vessels. The region of sclera closest to the uvea is called the lamina fusca, and contains a small number of pigment cells (melanocytes).

The vascular supply to the sclera
The sclera is relatively inactive metabolically, and therefore has minimal blood supply. The sclera receives nourishment from small capillaries in the episclera and also from the choroid, through branches of the long posterior ciliary arteries.

Innervation to the sclera:
Sensory innervation to the sclera is provided posteriorly by the short ciliary nerves (branch of the ophthalmic division of the trigeminal nerve) and anteriorly by the long ciliary nerves.

CORNEA

The cornea comprises the anterior 1/6th of the outer coat of the eyeball and ranges in thickness from 540um to 700um. The cornea is thinnest in the centre (0.5-0.6mm thick) and thicker at the periphery (0.7-1.0mm). With an anterior radius of curvature of approximately 7.8mm on average, the cornea makes up about two thirds of the refractive power of the eye. Structurally, the cornea consists of five layers, called the epithelium, Bowmans layer, stroma, Descemet's membrane and the endothelium (Figure 2.2).

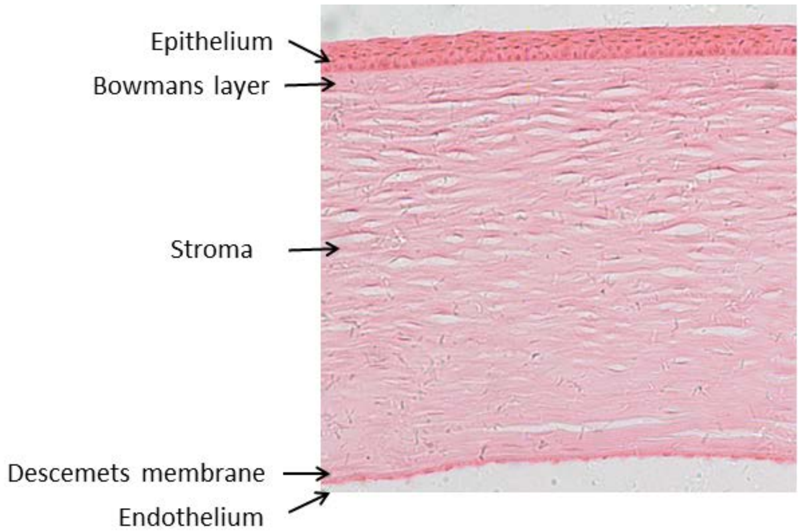
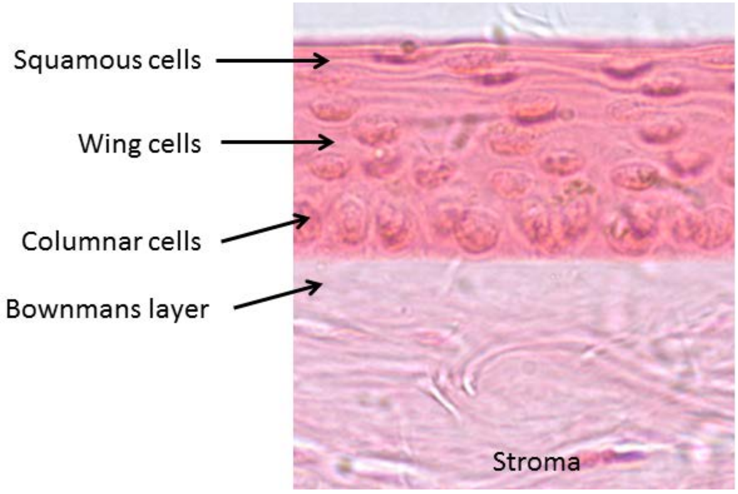


***Figure 2.2**. Haemotoxylin and eosin stained section of the monkey cornea showing the five histological layers.*

The **epithelium** forms the most external layer and interacts with the tear film. It consists of non-keratinized stratified squamous epithelial cells around 50 microns thick, and five to seven-cells deep. It is continuous with the epithelium of the bulbar conjunctiva at the limbus and acts as the main barrier to infection of the cornea (Figure 2.3). The most superficial layer of the 2-3 layers of squamous cells exhibit surface microvillae and microplicae (Figure 2.3), small finger like projections that serve as an adhesion site for the tear film and also increasing the surface area of epithelial cells to aid oxygen and carbon dioxide exchange. Tight junctions between epithelial cells act as a permeability barrier for the cornea.

Beneath the squamous cells are 2-3 layers of "wing cells", named for their lateral cells processes. These multiple layers are held together by numerous desmosomes, and intercellular communication is maintained through a system of gap junctions. The deepest of the epithelial layers is a single row of columnar basal cells, which generate a basement membrane for adhesion of the epithelium to the underlying Bowman's membrane. This single layer of cells is the only layer of the normal cornea in which mitotic division is observed. Continuous centripetal movement of basal cells from limbal stem cells to the centre, and then anteriorly through the stages of epithelial differentiation toward the corneal surface takes 7-8 days in total. Damaged areas are repaired both by mitosis and by lateral migration of surrounding cells (in flattened form) to cover denuded areas (e.g. following minor abrasion or refractive surgery).



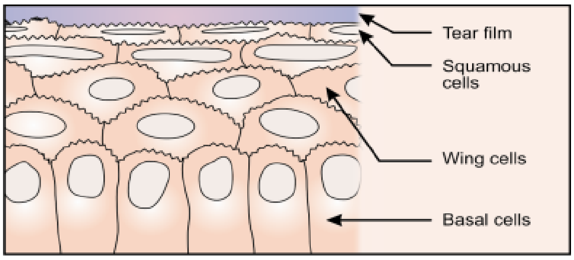


Figure 3.3. *(A) high magnification view of the corneal epithelium, showing the basal columnar cells, wing cells and squamous cells. (B) schematic diagram of the corneal epithelium.*

Bowman's layer is approximately 10-14 microns thick. It is acellular and composed of irregularly arranged collagen fibrils that have been embedded in a mucoprotein ground substance. Bowman's layer is acellular, and contains collagen fibrils of small diameter that, unlike the corneal stroma, are not ordered into bundles. Although Bowman's layer is sometimes referred to as a "membrane" it is more correctly considered a transition zone to the stroma.

The **stroma** forms about 90% of the total corneal thickness. It consists of thick dense collagen. The arrangement of collagen fibrils within the corneal stroma is unique and facilitates transparency of the cornea. Each collagen fibril is 20-25nm in diameter and run parallel to neighbouring fibrils. In addition, the spacing between each fibril is highly ordered. Groups of fibrils are called lamellae. The stroma consists of 200-250 flattened lamellae of collagen fibrils that are embedded in glycosaminoglycans and that run across the entire cornea. This laminated structure gives the cornea greater strength. Within the stroma, lamellae run at different angles to one another, although within each lamellae, the collagen fibrils run parallel to one another. Transparency for the cornea depends on the ordered arrangement of lamellae and the similarity of the collagen diameter. This highly ordered arrangement contrasts with that of the scleral stroma where the collagen fibrils differ in diameter and density (See Figure 2.5)

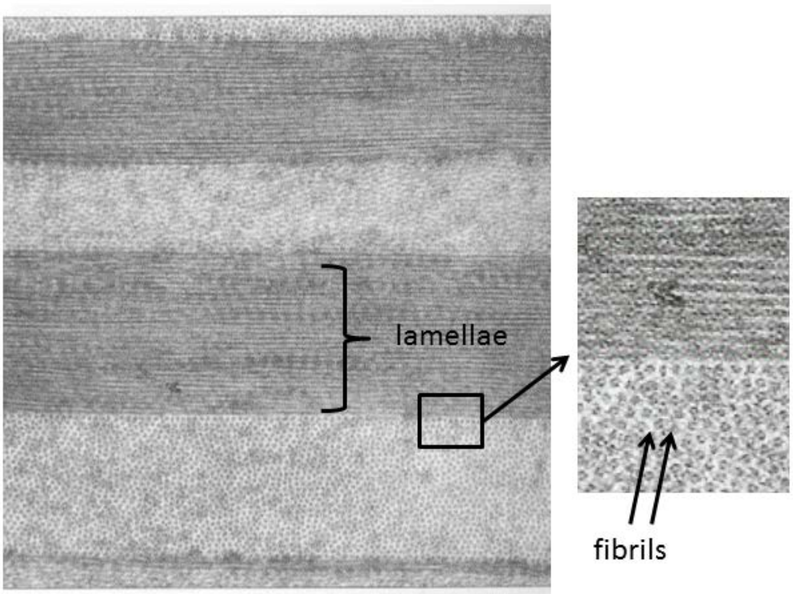


Figure 2.4 *Cross section of part of the corneal stroma viewed with an electron microscope. Packets of collagen fibrils called lamellae are seen. Each lamellae runs at a different angle to its neighbour.*

In addition to collagen fibrils, the corneal stroma also contains keratocytes, flattened cells that lie between lamellae. These cells actively form the collagen and extracellular matrix components of the stroma.

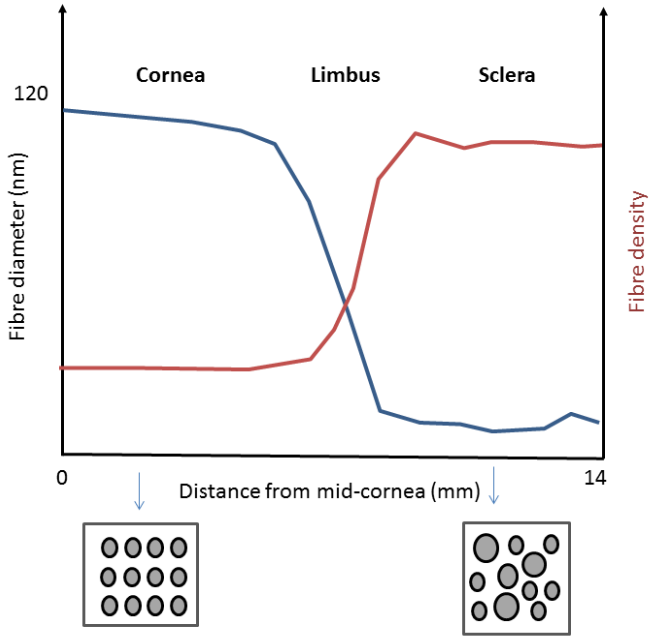


Figure 2.5: *Graph showing the change in diameter (red line) of collagen fibrils from the central cornea to the sclera and the change in density (blue line) of collagen fibrils from mid cornea to sclera. Within the cornea, collagen fibrils are all of a similar diameter and density. In contrast, in the sclera, the collagen diameter varies considerably, and show lower density.*

Descemet's Membrane is a 10 micron thick basement membrane produced continuously throughout life by the corneal endothelium (Figure 2.2). It displays strong elastic properties and terminates abruptly at the limbus. This terminus is visible clinically using a method called gonioscopy. Viewed using this instrument, the visible terminus of Descemet's membrane is called Schwalbe's line.

The endothelium

The endothelium is the inner most layer of the cornea that faces the anterior chamber. It is a single layer of interdigitating flattened hexagonal cells whose basal surface rests on Descemet's membrane (Figures 2.2 and 2.6). It is continuous with the endothelial cells that line the trabecular meshwork. Corneal endothelial cells are derived embryologically from neural crest cells and have a very limited capacity for proliferation. Their density gradually drops from 5000cell/mm^2 in the central cornea at birth to 1500-2000/mm^2 by middle age. The endothelium plays an essential role in transparency by maintaining corneal hydration and thickness. These functions depend on the barrier and fluid transport systems that reside within endothelial cells. The walls of the hexagonal endothelial cells have many ridges that interdigitate with their neighbour. This, together with a series of macula occludens rather than zonula occludens, located near the apical surface, results in a barrier that is slightly leaky. As a consequence, large molecules, nutrients like glucose and amino acids from the aqueous humour can pass across the endothelium into more anterior layers of the cornea. The endothelium is crucial for maintaining corneal hydration and thickness. This is achieved by a rich collection of metabolic pumps, such as Na+-K+-ATPase, that actively pump ions including sodium into the aqueous humour. Water passes down its concentration gradient from the cornea into the aqueous. Channels called aquaporins are also expressed on the surface of endothelial cells, and provide an additional route for fluid movement out of the cornea. The endothelium is rich in mitochondria and cellular organelles reflecting the high metabolic needs of these pumps and transporters.

The hexagonal shape of the corneal endothelium provides a means for ensuring that the entire cornea is covered without leaving gaps. There are unique contacts between adjacent cells that inhibit cellular proliferation. In addition, when cells are lost, remaining cells migrate to fill the gaps, resulting in cells of varying size or polymegathism.

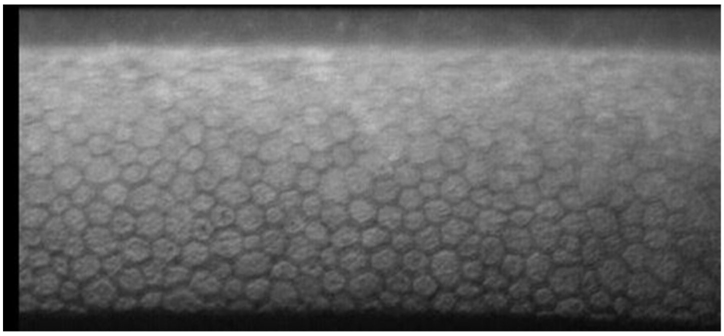


Figure 2.6 *The corneal endothelium viewed by specular microscopy. Small hexagonal shaped cells can be seen.*

Blood supply

The cornea is avascular and obtains nourishment by diffusion from the aqueous humour, and also from the capillary networks that reside in the conjunctiva and episclera.

Nerve supply

The cornea is 20-40 times more sensitive to touch than the tooth pulp, making even the most minor of touches to the cornea painful. The cornea is densely innervated by sensory nerves that originate from the long and short ciliary nerves and ultimately are branches of the ophthalmic division of the trigeminal nerve (Vth cranial nerve). As the sensory nerves pass into the cornea, they lose their myelin sheath. There are three main networks of sensory fibres within the cornea: one network is located mid stroma, a second network is located in Bowman's layer and send branches up into the epithelium where the third network of sensory fibres is located. The sensory nerves of the cornea respond to different types of stimulation by conveying a sensation of pain and are thus primarily nociceptors. Thermosensitive transient receptor potential (TRP) channels have been recently identified in the corneal epithelium, suggesting that some sensory receptors within the cornea may encode temperature.

THE CORNEOSCLERAL JUNCTION OR LIMBUS

Anteriorly, the sclera is continuous with the cornea at the limbus, or corneoscleral junction (Figure 2.7). Although the limbus is often considered the junction between the sclera and cornea, it has a number of important functions, especially in wound healing and nourishment of the peripheral cornea. At the limbus, the corneal epithelium thickens and transitions to form the conjunctival epithelium. The corneal stroma becomes continuous with the scleral stroma and Descemet's membrane ends. The corneal endothelium forms the endothelium of the trabecular meshwork. Beneath the conjunctival epithelium is the conjunctival submucosa, which is loose tissue that has no counterpart in the cornea. Tenons capsule lies just beneath the conjunctival submucosa.

The palisades of Vogt are radial projections of limbal epithelium and stroma that extend into the peripheral cornea. The epithelium in this area is thought to contain the corneal stem cells that are important for formation of the corneal epithelium.

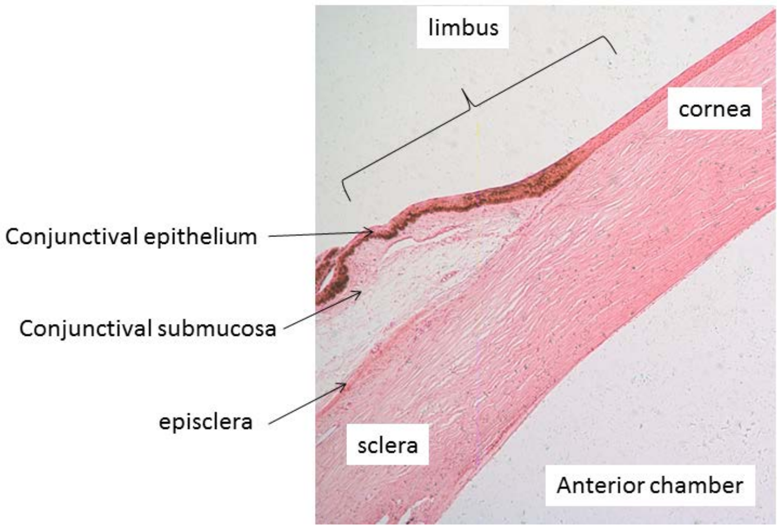


Figure 2.7.*Section through monkey eye showing the limbus, cornea and conjunctiva*